II. REMARKS

A. Status of the Claims

Claims 1-8 were originally filed with the case on June 2, 2005. A Restriction Requirement mailed on April 15, 2008, stated that the originally filed claims were directed to two patentably distinct inventions. In a Response to Restriction Requirement filed on September 15, 2008, Applicants elected the invention of Group I, that is, claims 1-4, directed to a method of treating glaucoma. All claims were rejected in an Office Action mailed on November 26, 2008. In a Response to Office Action filed on February 26, 2009, claims 1 and 4 were amended, claim 2 was cancelled and claims 5-8 were withdrawn from consideration. The outstanding Final Official Action, mailed on June 10, 2009, states that claims 3 and 4 are also withdrawn from consideration as not encompassing the elected species. Claim 1 is amended herein to correct typographical errors in the claim pointed out by the Examiner. No claims are cancelled or added. Claim 1 remains pending.

B. The Claims are Definite

The Action rejects claim 1 under Section 112, second paragraph, as being indefinite for failing to particularly point out the subject matter of the invention. The Action asserts that the chemical name for the compound SB 331750 contains typographical errors. The typographical errors contained within the chemical name for the compound SB 331750 have now been corrected. Applicants thank the Examiner for pointing out the errors in the Official Action. It is believed that the definiteness rejection as it relates to the typographical errors contained in the chemical name for the compound SB 331750 have been rendered moot by the amendments to the claim.

The Action further rejects claim 1 as being indefinite for use of the term "pyridoxal propionate derivatives". It is believed that the definiteness rejection based upon the term "pyrodoxal propionate derivatives" is moot in light of the amendments to claim 1.

Claim 1 is also rejected as being indefinite for inclusion of the term "cyanamides" twice. Claim 1 has been amended to delete one instance of the term "cyanamides." It is believed that the definiteness rejection based upon the term "cyanamides" is moot in light of the amendments to claim 1.

In light of the foregoing arguments, Applicants respectfully request that the definiteness rejections be withdrawn.

C. The Claims are Not Anticipated by Banerjee

Finally, the Action rejects claims 1-2 under Section 102(a) and 102(e) as being anticipated by Banerjee (U.S. Patent Pub. 2002/0160979). Banerjee is said to teach a method for inhibiting angiogenesis comprising administering a composition comprising a nucleoside, particularly tunicamycin. The conditions disclosed in Banerjee are said to include neovascular glaucoma. Applicants respectfully traverse.

The present invention is directed to a method for lowering intraocular pressure by topically administering to the eye of a patient a composition containing a cathepsin K antagonist. Banerjee does not describe methods for lowering intraocular pressure or topical ocular administration to the eye of a patient suffering from elevated intraocular pressure.

The objective of Banerjee is to inhibit angiogenesis, which it defines as "the growth of capillary endothelial cells which form new blood microvessels" (See ¶ [0064]). Furthermore, Bannerjee states that administration of the compound is typically systemic (See ¶ [0179]). The skilled artisan would not look to the art related to treatment of angiogenesis

when seeking a solution to treating elevated intraocular pressure because the cause of the damage to the tissues (i.e., elevated intraocular pressure vs. oxidative stress) and the tissues affected (i.e., inner retinal tissues vs. outer retinal tissues) differ significantly. Moreover, the mode of administration for treating elevated intraocular pressure (i.e., topical ocular administration) differs significantly from typical routes of administration for inhibiting neovascularization occurring in retinal tissues (i.e., local administration to the back of the eye).

It is well settled that, for a prior art reference to render a claim anticipated, that reference must set forth every element in the claim, either expressly or inherently. *Verdegaal Bros., Inc. v. Union Oil Co. of Cal.*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051 (Fed. Cir. 1987) (citing *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548, 220 U.S.P.Q. 193, 198 (Fed. Cir. 1983)). In other words, to support a rejection under section 102, a reference must show ***all*** features of the rejected claim(s). *Minnesota Mining & Mfg. v. Johnson & Johnson Orthopaedics, Inc.*, 976 F.2d 1559, 1569, 24 USPQ2d 1321 (Fed. Cir. 1992). The Federal Circuit has stated that "absence of a claim element from a prior art reference negates anticipation." *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 224 U.S.P.Q. 409 (Fed. Cir. 1984). Since Bannerjee lacks a teaching of lowering intraocular pressure, it cannot be said to anticipate the claimed invention.

In light of the foregoing arguments, Applicants respectfully request that the anticipation rejection based on Bannerjee be withdrawn.

D. Claim 1 is Patentable Over Banerjee

Finally, the Action rejects claim 1 as being obvious over Banerjee (2002/0160979). The Action acknowledges that Banerjee fails to teach a method of lowering intraocular pressure with the administration of a cathepsin K antagonist. Nevertheless, the Action takes

the position that it would have been obvious to utilize the method for inhibiting angiogenesis as taught by Banerjee comprising administering a composition comprising a nucleoside, particularly tunicamycin, for conditions such as neovascular glaucoma for lowering intraocular pressure resulting from angiogenesis factors. Applicants respectfully traverse.

The present invention is directed to a method for lowering intraocular pressure by topically administering to the eye of a patient a composition containing a cathepsin K antagonist (not a nucleoside). Banerjee contains no discussion of the use of cathepsin K antagonists for the treatment of anything, much less for lowering intraocular pressure.

The Action further argues that it is known in the art that neovascular glaucoma presents with intraocular pressure and that the intraocular pressure in neovascular glaucoma is a result of angiogenesis as evidenced by Hunter (U.S. Patent 5,886,026; U.S. Patent Application 2002/0192280) and Gurwood (Review of Optometry November 1999 Case Report). The Action asserts that the inhibition of the angiogenesis would inherently inhibit the cascade in neovascular glaucoma affecting the intraocular pressure which has been known and pursued in the art for many years.

In describing the occurrence of neovascular glaucoma, Hunter '026 explains that the increased intraocular pressure resulting from the neovascularization occurs after the neovascularization has progressed from the papillary margin, across the root of the iris, into the trabecular meshwork, eventually resulting in a fibrovascular membrane across the anterior surface of the iris. According to Hunter, this tissue "eventually" reaches the anterior chamber angle where it forms synechiae, which then coalesce, scar and contract to "ultimately" close off the anterior chamber angle. It is this scar formation that prevents adequate drainage of aqueous humor through the angle and into the trabecular meshwork,

resulting in an increase in intraocular pressure. (Col. 33, lines 47-62). Typically and ideally, neovascular glaucoma will be diagnosed in its early stages (i.e., before intraocular pressure is elevated) by high magnification slitlamp biomicroscopy, where it reveals small, dilated, disorganized capillaries on the surface of the iris. Later in the progression of the disease, it may be detected by progressive obliteration of the anterior chamber angle by fibrovascular bands. This would also occur prior to the elevation of intraocular pressure. According to Hunter, conservative therapies for the neovascularization may be effective at treating neovascular glaucoma while the anterior chamber angle is still open (i.e., before intraocular pressure is elevated). (Col. 34, lines 3-10). Hunter explains that "once the angle closes surgical intervention is required in order to alleviate the pressure." It is submitted that, after reading Hunter, the skilled artisan would be even more convinced that neovascular glaucoma must be treated by using anti-angiogenic factors before intraocular pressure becomes elevated as a result of the progression of the disease. Once intraocular pressure becomes elevated, the skilled artisan would be led to believe that one must perform surgery on the eye in order to decrease the intraocular pressure. In other words, the skilled artisan would not expect that anti-angiogenic factors would be effective in relieving elevated intraocular pressure resulting from neovascular glaucoma because the disease will have progressed too far by that point. The Hunter '290 application contains the same discussion of neovascular glaucoma that Hunter '026 contains.

Gurwood describes the treatment of a patient who was initially diagnosed with retinal vein occlusion of the left eye. At the initial diagnosis, the patient's intraocular pressure in both eyes was normal (see page 1). The patient was counseled to return for follow-up visits monthly for 6-8 months and to have a retinal consultation for treatment of the retinal vein

occlusion. The patient did not attend any follow-up visits and cancelled the appointment with the retina service. As a result, his neovascularization progressed. Gurwood states that "when the patient finally returned" intraocular pressure in his left eye had increased to 50 mm Hg. To lower the patient's pressure, a known IOP-lowering agent, timolol, was used to lower the pressure. Administration of timolol was said to lower the intraocular pressure to 27 mm Hg within 50 minutes. The patient was instructed to continue administering timolol twice daily. Panretinal photocoagulation was performed to arrest the neovascularization. Gurwood states that "medical therapy for neovascular glaucoma includes topical beta blockers, alpha2 agonists and oral carbonic anhydrase inhibitors.... Prompt panretinal photocoagulation can cause the neovascularization to regress and, thus, prevent glaucoma" (see page 4).

It is submitted that the standard of care for neovascular glaucoma known to the skilled artisan at the time of the invention, was to treat the neovascularization with methods known to inhibit neovascularization and to treat the elevated intraocular pressure with known IOP-lowering agents. Cathepsin K inhibitors were not "known IOP-lowering agents" at the time of the invention. The present inventors are the first to suggest their use for lowering IOP. The skilled artisan would not have expected that administering an agent to inhibit neovascularization would necessarily lower intraocular pressure, even intraocular pressure that is elevated as a result of neovascular glaucoma.

In light of the foregoing arguments, Applicants respectfully request that the obviousness rejection based on Bannerjee be withdrawn.

E. Conclusion

This is submitted to be a complete response to the outstanding Action. Based on the foregoing arguments, the claims are believed to be in condition for allowance; a notice of allowability is therefore respectfully requested.

The Examiner is invited to contact the undersigned attorney at (817) 551-4321 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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